

Applicant : Walter Callen et al.
Serial No. : 09/656,309
Filed : September 6, 2000
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Attorney's Docket No.: 09010-027003

REMARKS

Status of the Claims

Claims 31-42 and 52 are pending. In the present Response, claim 52 is canceled; claim 31 is amended; and new claims 53-88 are added. Thus, after entry of these amendments, claims 31-42 and 53-88 are presented for consideration.

Pursuant to the Office Action, claims 31-42 and 52 are rejected under 35 U.S.C. §112, first paragraph. Claims 31-42 and 52 are rejected under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse all outstanding rejections of the claims.

Support for the Claim Amendments

Claims have been amended and added to more particularly describe the invention. Support for the new claims can be found in originally filed claim 31. Accordingly, no new matter has been introduced by the instant amendments.

Issues under 35 U.S.C. §112, second paragraph

Claims 31-42 and 52 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

The Patent Office alleges that claim 31 (and, therefore, claims 32-42 and 52 which depend therefrom) is indefinite in that the language is confusing. Applicants have amended claim 31 and added claims 53-88 to clarify the language and alleviate the Patent Office's confusion. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, to the pending claims.

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Issues under 35 U.S.C. §112, first paragraph

Claims 31-42 and 52 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Patent Office alleges that the specification fails to describe the function of the method or the function of the variants that would be generated by the method.¹ Applicants respectfully direct the Patent Office's attention to page 16, lines 19-26, of the specification, where variants are defined. Applicants aver that the function of the claimed method is to generate a variant that encodes a polypeptide having polymerase activity. Moreover, the function of the variant is to encode a polypeptide having polymerase activity. Applicants have amended the claims to more clearly define the invention.

The Patent Office alleges that there is no disclosure of any particular structure to function/activity relationship in any disclosed species generated by such a method nor any guidance as to which if any residues should be modified. The Patent Office concludes that this lack of representative species as encompassed by the claims and alleges that Applicants have failed to sufficiently describe the claimed invention.² Applicants respectfully submit that the amended claims are drawn to methods of generating a variant encoding a polypeptide having polymerase activity. Applicants have described numerous protocols that one of ordinary skill in the art could use to practice the claimed invention. Applicants respectfully submit that, armed with the disclosure provided by the Applicants (*e.g.*, the nucleotide sequences that encode for polypeptides having polymerase activity, exemplary protocols that can be used in the practice of the claimed methods, and an assay to test for activity), one of ordinary skill in the art would be able to fully practice the claimed invention. For example, the skilled artisan could take a sequence having at least 70% identity to a sequence of SEQ ID NO:1 and which encodes for a polypeptide having polymerase activity, subject it to one of the exemplary techniques, such as

¹ Page 3, lines 22-23, of the Office Action.

² Page 3, line 23, to page 4, line 8, of the Office Action.

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error-prone PCR, and produce a variant. This variant can then be expressed and the resulting polypeptide can be tested for polymerase activity. Accordingly, Applicants respectfully submit that the specification sufficiently describes the claimed invention so that a skilled artisan would recognize that the inventors were in possession of the claimed invention.

Claims 31-42 and 52 are rejected under 35 U.S.C. §112, first paragraph, because while the specification enables for a method of generating a polymerase variant: comprising obtaining a nucleic acid sequence having at least 70% identity to SEQ ID NO:1 and sequences complementary thereto and modifying, deleting or adding one or more nucleotides in said sequence, wherein said variant maintains polymerase activity, it is alleged that the specification does not reasonably provide enablement for any method of generating any variant.³

The Patent Office alleges that the claims are so broad as to encompass all methods of generating variant polynucleotides which encode enzymes with polymerase activity as well as those which encode proteins with no function/activity and those which do not encode polypeptides/proteins, or modification and fragments of any nucleic acid sequence having 70% identity to SEQ ID NO:1 or fragments comprising at least 30 consecutive nucleotides thereof.⁴

Applicants respectfully submit that the amended and new claims are drawn to variants generated from nucleic acids having the sequence of SEQ ID NO:1, those having at least 70% identity to the sequence of SEQ ID NO:1, and fragments of those sequences, all encoding a polypeptide having polymerase activity, and not just any nucleic acid. From these, the skilled artisan can use recombinant and mutagenesis techniques that are known (examples of which are described in the specification) to generate variants that encode a polypeptide having polymerase activity. Accordingly, the claimed method does not contemplate the use of just any nucleic acid sequence having 70% identity to SEQ ID NO:1 or just any fragment, nor would the claimed method generate just any variant. Applicants respectfully submit that as acknowledged by the Patent Office on page 4, lines 13-17, of the Office Action, the method of generating a polymerase variant comprising obtaining a nucleic acid sequence having at least 70% identity to

³ Page 4, lines 12-18, of the Office Action.

⁴ Page 5, line 10, to page 6, line 21, of the Office Action.

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SEQ ID NO:1 and sequences complementary thereto and modifying, deleting or adding one or more nucleotides in said sequence, wherein the variant maintains polymerase activity is enabled by the specification.

The Patent Office alleges that the specification does not provide guidance on how the proteins' structure relates to its function. Applicants respectfully submit that the claimed invention is drawn to a method of generating variants using sequences of SEQ ID NO:1, sequences with 70% identity to SEQ ID NO:1 having polymerase activity and fragments having polymerase activity, and their complements. Applicants respectfully aver that the specification provides sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. Moreover, the Patent Office alleges that it is not routine in the art to screen for multiple substitutions or multiple modifications. Applicants respectfully disagree. Creating a polypeptide construct and testing its activity is the only sure way of knowing if the polypeptide has a particular function. While the use of computers to design polypeptides having a particular function is gaining wider usage, the only sure way of knowing if a polypeptide has retained its function is to create the polypeptide, such as by the claimed method, and test its function.

In light of the remarks and amendments set forth above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, to the pending claims.

CONCLUSION

Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

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Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no additional fees are necessitated by the present Response. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date: _____

1/22/2003



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Version with markings to show changes made

In the claims:

Claim 52 has been canceled.

Claim 31 has been amended as follows:

31. (Twice Amended) A method of generating a variant that encodes a polypeptide having polymerase activity comprising:

obtaining a nucleic acid comprising a sequence [as set forth in SEQ ID NO:1, sequences] having at least 70% identity [thereto] to the sequence set forth in SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or its complement [, sequences complementary to SEQ ID NO:1 or sequences having at least 70% identity to SEQ ID NO:1, and fragments comprising at least 30 consecutive nucleotides thereof,]; and

modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence, to generate a variant that encodes a polypeptide having polymerase activity.

Claims 53-88 have been added.